REMARKS

The Office Action of February 7, 2008, the first action following applicants' filing of an RCE, has been carefully reviewed, it being apparent to applicants that this action is substantially identically a repetition of the earlier final action, the points raised in applicants' reply to the final action not having been addressed.

The claims in the application thus remain as claims 1 and 3-17, including presently withdrawn claims 10-13. The claims define novel and unobvious subject matter for the reasons of record, and as further pointed out below. Accordingly, applicants again request favorable reconsideration and allowance.

For the third time, applicants ask why claim 13 is withdrawn when it is directed to the elected subject matter, and moreover is a linking claim. Applicants believe that they deserve the courtesy of an answer. Applicants also respectfully note that the MPEP requires an examiner to answer all points raised by an applicant in an applicant's reply.

Claims 1, 3-9, 14, 15 and 18 have been again rejected under Section 102 as allegedly anticipated by Iida. This rejection is again respectfully traversed, and for the reasons of record as set forth in the reply of September 20, 2007, the remarks of which are respectfully repeated by reference.

As can best be understood, the rejection appears to rely on a misinterpretation of applicants' own specification at page 36, example 2. Claim 1, and thus all of applicants' claims call for the amount of non-water-soluble light-shielding agent in the shell to be "5 to 30 wt%, based on the

total amount of all components constituting the shell". Iida does not disclose such subject matter and Iida does not make such subject matter obvious.

The rejection refers to column 3, lines 21-23 of Iida which specifically states as follows:

> It [the amount of white pigment used] is preferably 1.5% by wt or less, particularly 1.0% by wt or less, of the total amount of capsule shell components.

This in no way that a maximum of 1.5% white pigment in the shell corresponds to what is recited in applicants' claims as quoted above, namely "5 to 30 wt%" in the shell.

In the "Response to Arguments" portion of the final action mailed July 11, 2007, at page 5, the examiner stated as follows:

> Example 2 of the instant specification recites that a solution of 4 wt% titanium oxide contains 1 wt% titanium oxide. The Iida reference teaches titanium oxide up to 1.5% of the total amount of capsule shell components (see col. 3, line 23). Based on the formulation of instant Example 2, the Iida reference teaches a titanium oxide concentration of 6%,...

However, this statement and conclusion in the Final Action are simply **not correct**. Example 2 does not say that the "solution" contains 4 wt %.

Indeed, Recipe 2-1 in Example 2 in the present specification is for a shell-forming solution containing 1.0 wt% of titanium oxide (based on the total amount including water); and this is processed to provide a shell containing 4 wt% titanium oxide (quadrupled) by removing water from the solution.

In this regard, it should be noted that the shell-forming solution is not the resultant shell itself. In the

present invention, the concentration of the non-water-soluble light-shielding agent is calculated based on the total amount of all components constituting the shell, not the material of the solution of the shell which includes liquid carrier, e.g. water, which is removed to from the shell. In fact, the present specification defines the total amount as "the sum of the amounts of all capsule shell components, except for liquid (i.e., water and volatile media) added to prepare a shell-forming solution (please refer to page 20, line 4-9 of the present specification).

Why the PTO has not answered or rebutted applicants' previous remarks in this regard is not understood. If the examiner does not answer or rebut the arguments of an applicant, then how can that applicant understand the reasons the examiner has for maintaining the examiner's position. MPEP 707.07(f) is explicit in this regard, stating:

> In order to provide a complete application file history and to enhance the clarity of the prosecution history record, an examiner must provide clear explanations of all actions taken by the examiner during prosecution of an application.
>
> ***
>
> Where the applicant traverses any rejection, the examiner should, if he or she repeats the rejection, take note of the applicants' argument and **answer the substance of it.** [emphasis added]

If the examiner continues to maintain the rejections based on a faulty understanding of what the reference discloses and teaches, which applicants have clearly pointed out, then applicants at least deserve that the examiner "answer the substance of" applicants' arguments.

Applicants must say, although with respect, that applicants find the examiner's description of Example 2 as quoted above puzzling and somewhat incoherent. A correct reading of example 2 is that the 4 wt% of titanium oxide is the concentration of titanium oxide in the shell, not in the shell forming solution. Nevertheless, to make example 2 even more clear, applicants have amended example 2 above so that it cannot be misunderstood.

Applicants can only assume in maintaining the rejection that the examiner projectively applied the original language of example 2 to the understanding that the concentration of titanium oxide of "1.5% by wt" as disclosed in Iida to mean that the concentration in Iida is 6% titanium oxide, regardless of there being no such teaching in Iida and regardless that the concentration recited by Iida is in the solid shell, even though Iida specifically says it "is preferably 1.5% by wt or less... **of the total amount of the capsule shell components**", not of the liquid composition used to form the shell which includes substantial amounts of liquid which do not end up in the final product.

Amendments made above to page 36 of applicants' specification should ensure that the examiner will understand that recipe 2.1 is for the shell-forming solution including 1 wt % titanium dioxide and 75 wt % water, and this is processed to a shell containing 4 wt % titanium oxide by removing the water from the solution.

Returning again to the Iida disclosure, it should be clear that the percentages in the solution used to form the shell must be differentiated from the percentages in the dry shell, just as that same distinction has been made above and previously with respect to applicants' specification and particularly example 2.

As pointed out in the remarks of the reply filed September 20, 2007, Iida states at column 3, lines 25-27: "As used herein, the total amount of capsule shell components means the amount of the materials of capsule shell excluding water" (emphasis added); and describes at column 6, lines 51-54: "In Table 1 above, each value represents the charge (expressed in % by weight) of each component relative to the total amount of the materials of the shell (excluding water)" (emphasis added).

In this way, both in the present invention and in Iida, the amount of water is not taken into account when the concentration of the **shell** is calculated (that is, the concentration is calculated based on the total weight of a shell which does not include the water). The same is also true for the concentration of titanium oxide "1.5 % by weight" described in column 3, line 23 of Iida. Therefore, this figure of "up to 1.5%" means just that, not a converted quadrupled figure of 6%. It is absolutely clear that this figure of 1.5 wt% is not included in the range of 5-30 wt% of the present invention.

Although applicants have carefully reviewed Iida, applicants have been unable to find any description which can provide a rational reason (or enable those skilled in the art) to quadruple 1.5% to 6%.

Accordingly, the present invention is not described in Iida, and is clearly novel over Iida.

As previously noted, applicants calculated the concentration of titanium oxide of a shell-forming solution of Example 5 of Iida before preparing a shell. The calculated figure is about 0.5 wt% based on the total amount including water. This is almost one half of the concentration based on the total amount excluding water (1.00% according to Table 1).

With regard to the amount of water and the other components, applicants relied on the conditions (e.g. 50 parts by weight of purified water) described in Example 1.

Accordingly, with no changes at all in claim 1, such claim (and all the claims which depend therefrom) define novel subject matter over Iida. The rejection based on §102 should be withdrawn for this reason alone, and such is again respectfully requested.

Claims 1, 3-9, 14-17 and 19 have also been rejected as obvious under Section 103 from Iida. This rejection is again respectfully traversed, and again for the reasons of record which are respectfully repeated by reference.

First, and simply for the record, applicants respectfully repeat that rejections under both Sections 102 and 103 of the same claims on the basis of the same reference are inconsistent because the subject matter cannot be both anticipated by a reference and obvious from that same reference, noting the express language of Section 103. Nevertheless, this is merely a formality. Applicants having shown above and previously that Iida does not anticipate applicants' claims, applicants now address the alleged obviousness of the present invention from a consideration of Iida.

The light-stabilized soft capsule shell of the present invention contains a very high amount of a non-water-soluble light-shielding agent, namely 5-30 wt% based on the total amount of all components constituting the shell. This is not an arbitrary amount, but is absolutely critical to the present invention, such as pointed out in the paragraph spanning pages 3 and 4 of applicants' specification.

> As a result of extensive and intensive efforts directed to recipes for capsule

> shell of soft capsule formulations and methods for their manufacture, the inventors of the present invention have developed a recipe for capsule shell including a high content of a non-water-soluble light-shielding agent ... . They also have found that this ... allows a sufficient reduction in light transmittance even for soft capsule shells less than 200 μm in thickness, thus enabling light stabilization of soft capsule formulations containing a light-unstable medicament even with a smaller capsule size.

As described in this paragraph, the high content of a non-water-soluble light-shielding agent allows a sufficient reduction in light transmittance even for soft capsule shells less than 200 μm in thickness, thus enabling light stabilization of soft capsule formulations containing a light-unstable medicament even with a smaller capsule size. What an applicant states in his or her specification is to be accepted by the PTO in the absence of evidence or good reasoning to the contrary, neither of which are present in this case.

That the range is critical is confirmed by the test examples in applicants' specification, and particularly Example 2, the results of which are illustrated in Fig. 4. As claimed, the minimum content of non-water-soluble light-shielding agent is 5%, and **Fig. 4 shows that with only 4%, the results were relatively poor.** Also see applicants' specification in the paragraph spanning pages 19 and 20, which provides support for claims 16 and 17, which claims are patentable for the same reasons as the other claims as pointed out herein.

The PTO relies on Iida which teaches the use of white pigment, e.g. titanium oxide, to protect the medicament within the capsule from light and heat, but wherein the amount

of such pigment is **very low** compared with what is claimed. Thus, and again at column 3, lines 21-23, Iida states:

> It [the amount of white pigment used] is preferably 1.5% by weight or less, particularly 1.0% by weight or less, of the total amount of capsule shell components.

There is not the remotest hint to one of ordinary skill in the art to increase the quantity of shielding agent to such a significantly greater degree than what is taught by Iida. Such a teaching comes only from applicants' own specification, which was not available to the person of ordinary skill in the art at the time the present invention was made. Applicants respectfully submit that it is not fair and not proper to use an applicants' own specification as a teaching to modify the prior art in a way which the prior art itself does not teach, and this is moreover contrary to MPEP 2143..

The PTO relies upon *In re Aller*, 105 USPQ 233, 235 (CCPA 1955) to urge that applicants' selection of a vastly greater amount of shielding agent than taught in the prior art would have been obvious due to routine experimentation, but this is not so. Whereas the PTO deems the claimed quantity of shielding agent to be a mere optimum, this is in fact the required range necessary to achieve the required degree of shielding, as proven in the aforementioned example 2.

In *Aller*, the court held that when the general conditions of a claim are disclosed in the prior art, in that case a temperature range, it is not inventive to discover optimum or workable ranges by routine experimentation. But *Aller* also makes clear that "Changes such as these may impart patentability to a process if the particular ranges claimed produce a new and unexpected result which is different in kind and not merely in degree from the results of the prior art"

[citation omitted; 105 USPQ at 235]. See also *In re Antonie*, 195 USPQ 6 (CCPA 1977), where the rejection was reversed. Applicants have indeed produced a new and unexpected result which is different in kind, as demonstrated in Fig. 4 where even 4% of the shielding agent was insufficient, such 4% being several times the amount suggested in the relied upon prior art.

Moreover, please see *In re Yates*, 211 USPQ 1149 (CCPA 1981), where the holding in *Aller* was explained and the rejection was reversed. *Yates* involved claims for a process for oxidizing an olefin to an unsaturated aldehyde. The claim specified that a gaseous mixture of olefin and molecular oxygen is combined with a catalyst of specified composition at an elevated temperature to convert from 25 to 80% of the olefin to product, maintaining the unsaturated acid content of the product at less than 2% of the unsaturated aldehyde content. The prior art, Okada, disclosed a process for catalytically oxidizing olefins to unsaturated aldehydes and acids, which generally paralleled the *Yates* process. However, Okada did not disclose the ratio of acid to aldehyde produced, nor did it disclose the relation of the degree of conversion to percentage production of acids or exemplify processing having a degree of conversion greater than 80%.

Okada showed examples of olefin to aldehyde oxidation reactions using various oxidation catalysts similar to those used by Yates. In the examples, the percentage of acid was generally in the 3-10% range, and there was no clear relationship between conversion and acid production. The court concluded that the examples, taken as a whole, supported the argument that a person of ordinary skill in the art would not have expected the degree of olefin conversion to be result

effective for the percentage production of unsaturated acid (211 USPQ at 1151).

As in *Yates*, the prior art presently relied upon does not lead the person of ordinary skill in the art to use the vastly increased amounts of shielding agent claimed, or the vastly improved results achieved thereby.

Moreover, applicants are aware of extrinsic evidence which teaches that the content of a non-water water-soluble light-shielding agent, e.g. titanium dioxide, in a soft capsule shell **should not exceed 1%**. Thus, applicants previously filed a copy of a article in the name of Matsuda et al, *Chem. Pharm. Bull.*, 28(9), 2665-2671, 1980, which contains such a teaching, noting especially the last paragraph on page 2669, which clearly says that "the effect of concentration seems to level off somewhat above 1% addition, ..."

Also see Fig. 2 at page 2667, exhibiting changes in light transmittance of gelatin films having 80 μm of thickness observed within a wavelength of 290-410 nm, when varying the content of titanium oxide (0, 0.5, 1.0, and 1.5 wt%) in the gelatin films; and Fig. 4 at page 2667 of the document, exhibiting changes in average light transmittance of gelatin films having 50-150 μm of thickness observed within a wavelength of 290-450 nm, when varying the content of titanium oxide (0, 0.5, 1.0, and 1.5 wt) in the gelatin films.

Both figures show that light transmittance of gelatin films decreases as the titanium oxide content increases. **However, these figures also show that a degree of the decrease in the light transmittance becomes smaller as the titanium oxide content increases.** This will be apparent when comparing distances between light transmittance curves in the figures for 0 wt% and 0.5wt%, for 0.5 wt% and 1.0 wt%, and for 1.0 wt% and 1.5 wt% of the titanium oxide content. The

distance between the curves for 1.0 wt% and 1.5 wt% is particularly very short. Thus, Matsuda et al conclude in the abstract that **"the effect of concentration seemed to disappear above 1% addition"**. This document is part of the prior art "as a whole", and cannot be properly ignored by the PTO.

Therefore, the skilled worker in the art would not have been motivated by the disclosure of the prior art "as a whole", including this document, to make a soft capsule having a shell of 80 μm (this value also means 200 μm or less, which is recited in claim 1 of the present application) in thickness, which contains titanium dioxide in an amount of 1 wt% or more of the weight of the shell, let alone more than 5 wt%.

Contrary to the teaching of Matsuda et al and Iida et al, the present inventors found that the light shielding effect resulting from an increase in the content of titanium dioxide does not reach a plateau even when the content very substantially exceeds 1 wt%. This finding is specifically supported by working examples in the present specification. Especially, Fig. 4 shows that, even in the range of 4% to 20% titanium oxide content, which is vastly higher than 1%, there is not any minimum limit for light remittance, but that the light-shielding effect is enhanced as the titanium oxide content becomes higher. The present invention is based on this new finding. Iida neither describes nor teaches this finding. Therefore, the present invention, having the feature that 5-30 wt% of a non-water-soluble light-shielding agent is contained in the shell, would not have been obvious from Iida.

Also, it should be noted that it was difficult to produce a soft capsule shell having a high content of a non-water-soluble light-shielding agent, e.g., titanium oxide, with a practical satisfactory quality. Specifically, as

described in pages 24-25 of the present specification, to reduce deviations in the light-shielding effect of the shell among soft capsule formulations, it is necessary to keep uniform dispersion of a non-water-soluble light-shielding agent in a shell-forming solution from the beginning to the end of encapsulation. However, when preparing a soft capsule shell having a high content of a non-water-soluble light-shielding agent, it was difficult to maintain successful dispersion of the agent, even when the agent was added to a solution of a gelling agent (e.g. gelatin) and then treated by ultrasonication.

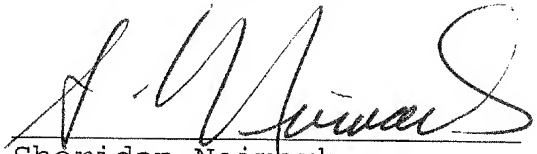
This problem was a barrier to production of a soft capsule shell having a high content of titanium oxide, with a practically satisfactory quality. To resolve this problem, the present inventors utilized a method of dispersing a non-water-soluble light-shielding agent in water by ultrasonication before being added to a solution of a gelling agent, instead of adding a water suspension of titanium dioxide to a solution of a gelling agent before ultrasonication. In other words, ultrasonication is conducted in a middle step of preparing the solution for the soft capsule shell, not in the last step. This fact should be considered when evaluating the unobviousness of the present invention.

Withdrawal of the rejection is in order and is respectfully requested.

All issues raised in the Office Action are addressed above. Respectfully, the PTO has not met its burden of establishing either anticipation or obviousness, and therefore the rejections should be withdrawn and the claims allowed. Such is respectfully requested.

Respectfully submitted,

BROWDY AND NEIMARK, P.L.L.C.
Attorneys for Applicant

By 
Sheridan Neimark
Registration No. 20,520

SN:tdd
Telephone No.: (202) 628-5197
Facsimile No.: (202) 737-3528
G:\BN\Y\YUAS\Mizutani3\pto\2008-05-07AMD FRMPCTFormat.doc